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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/057,323	01/25/2002	Harry R. Davis	CV01489K	1525

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PATENT DEPARTMENT (K-6-1, 1990)
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EXAMINER	
HUI, SAN MING R	
ART UNIT	**PAPER NUMBER**
1617	

DATE MAILED: 03/01/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/057,323	DAVIS ET AL.	
	Examiner	Art Unit	
	San-ming Hui	1617	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *23 November 2003*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-101* is/are pending in the application.

4a) Of the above claim(s) *See Continuation Sheet* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-4,11-13,21,28,32,34,37-40,42,43,47,48,83,86,100 and 101* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date 5/1/03, 5/16/03, 12/1/03, 10/31/03, 4/10/03, 4/2/03, 3/11/03, 12/23/02, 8/26/02
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

Continuation of Disposition of Claims: Claims withdrawn from consideration are 5-10,14-20,22-31,33,35,36,41,44-46,49-82,85 and 87-99.

DETAILED ACTION

Election/Restrictions

Applicant's election with traverse of the invention of Group I, claims 1-34, 37-40, 42-48, 53-54, 56, 58-59, 61, 63-64, 66, 68-69, 71, 73-74, 76, 78-79, 81, 83-84, 86, 88-91, and 93-101, in response filed November 21, 2003 is acknowledged. The traversal is on the ground(s) that a linking claim encompassing the scope of both pharmaceutical composition and the method of using such composition and therefore, it is improper to restrict the composition and the treatment method. This is not found persuasive because there is no linking claim recited in the instant application. Furthermore, even though a linking claim is recited, the restriction would still be considered proper since search fields for the composition and the method of using such composition are different and diverse (See restriction requirement in the previous office action).

Applicant's election of the species of fenofibrate, ezetimibe, and niacin, in response filed November 21, 2003 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

The requirement is still deemed proper and is therefore made FINAL.

Claims 35-36, 41, 49-52, 55, 57, 60, 62, 65, 67, 70, 72, 75, 77, 80, 82, 85, 87, and 92 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being no allowable generic or linking claim.

Applicant timely traversed the restriction (election) requirement in response filed November 21, 2003.

Claims 5-10, 14-20, 22-27, 28-31, 33, 44-46, 53-54, 56, 58-59, 61, 63-64, 66, 68-69, 71, 73-74, 76, 78-79, 81, 88-91, and 93-99 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected species, there being no allowable generic or linking claim. Election was made **without** traverse in response filed November 21, 2003.

Claims 1-4, 11-13, 21, 28, 32, 34, 37-40, 42, 43, 47-48, 83, 86, and 100-101 have been examined herein to the extent they read on the elected invention and species.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 21 and 32 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the additional cardiovascular agents disclosed in pages 66-69 of the instant specification, does not reasonably provide enablement for other cardiovascular agents. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims. In the instant case, the specification fails to provide information that would allow the skilled artisan to practice

the instant invention without undue experimentation. Attention is directed to *In re Wands*, 8 USPQ2d 1400 (CAFC 1988) at 1404 where the court set forth the eight factors to consider when assessing if a disclosure would have required undue experimentation. Citing *Ex parte Forman*, 230 USPQ 546 (BdApls 1986) at 547 the court recited eight factors:

1) the quantity of experimentation necessary,

2) the amount of direction or guidance provided,

3) the presence of absence of working examples,

4) the nature of the invention,

5) the state of the prior art,

6) the relative skill of those in the art

7) the predictability of the art, and

8) the breadth of the claims.

Applicant fails to set forth the criteria that define "cardiovascular agents". Additionally, Applicant fails to provide information allowing the skilled artisan to ascertain these compounds without undue experimentation. In the instant case, only a limited number of "cardiovascular agents" examples are set forth, thereby failing to provide sufficient working examples. It is noted that these examples are neither exhaustive, nor define the class of compounds required. The pharmaceutical art requires each embodiment to be individually assessed for physiological activity. There is no guidance as to how to select the suitable agents for use in the instant invention. The instant claims are so broad that they read on all "cardiovascular agent(s)", necessitating

an exhaustive search for the embodiments suitable to practice the claimed invention. Applicants fail to provide information sufficient to practice the claimed invention, absent undue experimentation.

Claims 34, 47, 84, and 101 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. In the instant case, the claims herein are not enabled for the prevention of vascular diseases, obesity, diabetes, and other diseases recited herein.

The claims are directed to a composition of preventing the vascular conditions comprising sterol absorption inhibitor, PPAR activator, and nicotinic acid derivatices. The specification fails to adequately teach how to use the herein claimed composition to prevent the any vascular event. It is well-known in the state of the art that vascular conditions encompass various cardiovascular disorders such as hypertension, acute myocardial infarction, unstable angina, endocarditis, and even arrhythmia, such as ventricular fibrillation. These conditions are caused by various etiologies. See, Merck Manual, 16th ed., 1992, page 365-367, table of content for cardiovascular disease. Please note that even a basic reference, such as Merck Manual, has over 200 pages of information with regard to cardiovascular disease. The instant claims are so broad that it encompasses the method of preventing **all** vascular disorders. The current known treatments of these disorders depends on the patient populations and the severity of the

disorders. Some of the disorders, such as primary hypertension, have no known etiology (See Merck manual, page 413). Thus, it is clear from the evidence of the Merck Manual that the ability to prevent vascular condition is highly unpredictable and has met with very little success. Applicants have not provided any convincing evidence such as working examples that their claimed invention is indeed useful as preventive for the first occurrence of vascular condition and have not provided sufficient guidance to allow one skilled in the art to practice the claimed invention without undue experimentation. In the absence of such guidance and evidence, the specification fails to provide an enabling disclosure.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1-4, 11-13, 21, 28, 32, 34, 37-40, 42, 43, 47-48, 83, 86, and 100-101 are rejected under 35 U.S.C. 103(a) as being unpatentable over Rosenblum et al. (US Patent 5,846,966) and Medical Letter (The Medical Letter on Drugs and Therapeutics, 1998, 40;1030:68-69).

Rosenblum et al. also teaches the elected compound herein, ezetimibe, useful for reducing cholesterol and the risk of artherosclerosis (See the abstract, also col. 32, Example 6, Compound 6A, and col. 40, line 52 particularly).

Medical Letter teaches fenofibrate as useful in reducing serum cholesterol level (See page 68 – 69).

The references do not expressly teach a composition containing fenofibrate and ezetimibe together.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to incorporate both ezetimibe and fenofibrate together in a single composition.

One of ordinary skill in the art would have been motivated to incorporate both ezetimibe and fenofibrate together in a single composition. The prior art teaches that both ezetimibe and fenofibrate as useful in reducing serum cholesterol individually. Therefore, combining two agents, which are known to be useful to reduce serum cholesterol individually, into a single composition useful for the very same purpose is *prima facie* obvious (See *In re Kerkhoven* 205 USPQ 1069).

Claims 21 and 32 are rejected under 35 U.S.C. 103(a) as being unpatentable over Rosenblum et al. and Medical Letter as applied to claims 1-4, 11-13, 21, 28, 32, 34, 37-40, 42, 43, 47-48, 83, 86, and 100-101 above, and further in view of Katzung (Basic & Clinical Pharmacology, 6th ed., 1995, page 529).

Rosenblum et al. and Medical Letter suggest a composition containing fenofibrate and ezetimibe.

Rosenblum et al. and Medical Letter do not expressly teach the composition contains niacin.

Katzung teaches niacin as useful for lowering cholesterol (See page 529, col. 1).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to incorporate niacin into the fenofibrate – ezetimibe composition.

One of ordinary skill in the art would have been motivated to incorporate niacin into the fenofibrate – ezetimibe composition. All three ingredients, i.e., niacin, fenofibrate, and ezetimibe, are known as useful in reducing cholesterol. Therefore, combining two or more agents, which are known to be useful to reduce serum

cholesterol individually, into a single composition useful for the very same purpose is *prima facie* obvious (See *In re Kerkhoven* 205 USPQ 1069).

Any inquiry concerning this communication or earlier communications from the examiner should be directed to San-ming Hui whose telephone number is (703) 305-1002. The examiner can normally be reached on Mon 9:00 to 1:00, Tu - Fri from 9:00 to 6:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sreeni Padmanabhan, PhD., can be reached on (571) 272-0629. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

San-ming Hui
Patent Examiner
Art Unit 1617